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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GUZO, DAVID	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,961	CLARKE ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *31-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/8/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 31-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/15/04.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences in the specification and Drawings have not been identified by the appropriate SEQ ID NO identifiers. Any response to this Office Action which does not include complete compliance with the Sequence Rules will be considered non-responsive.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-5, 8-15 and 20-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Henderson et al.

Applicants claim a viral vector (which can be an adenoviral vector) having at least one interfering genetic element (which can be any cis-acting element in the vector, such as an adenoviral ITR element) and comprising at least one transcription unit, wherein at least one insulating sequence (which can be a termination signal or polyadenylation signal sequence) is located 5' to the transcription initiation site of said transcription unit and 3' to said interfering genetic element and wherein said vector comprises a therapeutic gene, 5' and 3' ITRs, an adenoviral packaging signal and wherein the transcription unit is an essential adenoviral gene such as E1a, E1b, E2 or E4 operably linked to a tissue-specific transcriptional regulatory sequence such as a promoter or enhancer selected from viral enhancers, or AFP, PSA, hKLK2 or CEA promoters. Applicants also claim viral particles comprising the recited vectors and eukaryotic cells transfected with said viral (adenoviral) vector particles. The examiner is interpreting the claimed viral vectors as follows. The vectors read on any adenoviral vector which has at least one interfering genetic element (such as an ITR) and comprising at least one transcription unit (a coding sequence), wherein at least one insulating sequence (a termination sequence or polyadenylation signal sequence) is located 5' to the transcription initiation site of said coding sequence and 3' to the termination sequence or polyadenylation sequence.

Henderson et al. (US Patent Publication 2004/0241857, published 12/2/04, effective filing date of 9/10/98, see whole document, particularly Fig. 1; Fig. 8-9; Fig. 11; Fig. 13; [0060]-[0065]; [0073]-[0074]; [0086]; [0118]-[0130]; [0140]-[0145]; [0150]-[0159]; [0170]; [0198]; [0206]-[0208]; [0230]; [0246]; [0259]; [0272]; [0275]; [0279]-[0281])

recites adenoviral vectors which contain at least one interfering genetic element (an ITR) and comprising at least one transcription unit (i.e. a coding sequence for E1b proteins) wherein at least one insulating sequence (a termination sequence or polyadenylation signal sequence for the E1a gene) is located 5' to the transcription initiation site of the E1b gene and 3' to the interfering genetic element (the adenoviral left hand ITR). Henderson et al. also recites adenoviral vectors further comprising therapeutic genes such as those encoding antigens, cytokines, cytotoxic proteins for killing cancer cells, etc.), 5' and 3' ITRs, a deleted E3 region, an adenoviral packaging signal and wherein the transcription unit is an essential adenoviral gene such as E1a or E1b, etc. operably linked to a tissue-specific transcriptional regulatory sequence such as a promoter or enhancer selected from viral enhancers, or AFP, PSA, hKLK2 or CEA promoters. Applicants also claim viral particles comprising the recited vectors and eukaryotic cells transfected with said viral (adenoviral) vector particles. In adenoviral vectors CN234 and CN224, for example, the insulating sequence (termination signal for the E1a gene) is located within 3,000 nucleotides 5' to the transcription initiation site of the E1b transcription unit. With regard to instant claim 15, Henderson et al. recites deletions at positions 194 to 316 (see paragraphs [206]-[219]) which are 5' to the termination signal sequence at the 3' end of the E1a gene. Henderson et al. therefore teaches the claimed invention. With regard to instant claims 13-14, since the adenoviral vectors of Henderson et al. contain the adenoviral 5' ITR and a packaging signal (both of which fall within applicants' definition of interfering genetics elements), it must be assumed that they contain the interfering genetic elements contained between

nucleotides –141 to -305 of the E1a transcription start site (this would be in the packaging signal sequence).

Claims 1-2, 4-6, 8-15, 20-22 and 27-30 rejected under 35 U.S.C. 102(e) as being anticipated by Tikoo et al.

Applicants' invention is as described in the above 102(e) rejection over Henderson et al. Additionally, in claim 6, applicants recite that the insulating sequence is a SV40 late polyadenylation signal sequence.

Tikoo et al. (US 6,458,586, issued 10/1/02, filed 11/1/99, see whole document, particularly Figs. 6-9, Columns 11-13, Examples 4-7) recites bovine adenoviral vectors (BAVs) comprising at least one interfering genetic element (ITRs) and comprising at least one transcription unit (i.e. an E1b gene or E4 gene, etc.) wherein at least one insulating sequence (i.e. a termination sequence or polyadenylation signal sequence) is located 5' to the transcription initiation site of said transcription unit and 3' to the left hand ITR and a therapeutic gene. Tikoo et al. recites BAVs further comprising 5' and 3' ITRs, a packaging signal, a gene essential for replication (i.e. E1b or E4, etc.), SV40 late polyadenylation signal sequence operably linked to a bovine herpesvirus type I (BHV-1) glycoprotein D (gD) coding sequence inserted into the deleted E1a gene locus and comprising a deleted E3 region as well as recombinant BAV particles and eukaryotic cells transfected with the viral particles. With regard to the limitation of claim 2, it is noted that the termination sequence at the end of the gD gene is less than 3,000 nucleotides 5' to the transcription initiation site of the E1b transcription unit and the

deletion of the E1a gene represents a deletion 5' to the termination sequence. Tikoo et al. therefore teaches the claimed invention.

Claims 1-5, 8-15, 20-22 and 27-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Perricaudet et al.

Applicants' invention is as described above. Additionally, in claim 3, applicants recite the insulating sequence is located 5' to the transcription initiation site of the first transcription unit from the 5' end of the vector.

Perricaudet et al. (US 6,420,170, issued 7/16/02, filed 12/19/97, see whole document, particularly adenoviral vectors comprising 5' and 3' ITRs, a packaging signal, a gene essential for replication (i.e. E2, E4, etc.) and further comprising at least one interfering genetic element (an ITR), a transcription unit (such as a transgene comprising a promoter and polyadenylation sequence or a native adenoviral transcription unit) wherein at least one insulating sequence (a negative regulatory element, see column 10, lines 17-34) is located 5' to the transcription initiation site of the transgene and 3' to the ITR. The transgene can comprise a termination signal sequence which is located less than 3,000 nucleotides 5' to the transcription initiation site of an adenoviral gene such as the pIX gene in the adenoviral sequence 3' to the location of the transgenes if said transgene is located in a deleted E1a or E1b gene locus. Perricaudet et al. therefore teaches the claimed invention.

Claims 1-5, 11, 16-18, 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Ayares et al.

Applicants' invention is as described above. In addition, applicants, in claims 16-18, recite that the adenoviral vector has a deletion in the packaging signal 5' to the termination signal sequence such that the packaging signal becomes non-functional and that said deletion spans at least nucleotides 103-551 or 189-551.

Ayares et al. (US 2001/0046965, published 11/29/01, effective priority date to 3/4/97, see whole document, particularly the Abstract, Figs. 7 and 9, paragraph [25]) recites an adenoviral vector with 5' and 3' ITRs, a deleted E1 region and a deleted packaging signal (as a result of flanking the packaging signal with loxP sites and growing the vector in Cre producing cells) wherein a deletion of the packaging signal and E1 regions would encompass a deletion of nucleotides 103-551 (defining the packaging signal and 5' region of the E1a gene). The remainder of the adenoviral genome 3' to the E1 deletion contains the first and subsequent transcription units of the adenoviral genome as well as a insulating sequence (i.e. a polyadenylation signal or termination sequence) at the 3' end of the first adenoviral gene 3' to the E1 deletion and wherein the adenoviral vector comprises an essential gene such as E4 or E2. It is also noted that the loxP site in the Ad5(pBHG10) vector falls within applicants' definition of an insulating sequence since it serves (when in the presence of Cre) to insulate genes downstream from the actions of the packaging signal sequence (an interfering genetic element) by deleting said packaging signal. Ayares et al. therefore teaches the claimed invention.

Claims 1-5, 8-15, 19-22 and 27-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Lieber et al.

Applicants' invention is as described in the above 102(e) rejections. Additionally, in claim 19, applicants recite the limitation of locating the packaging signal 3' to the termination signal sequence.

Lieber et al. (US Patent 6,686,196, issued 2/3/04, effective filing date 5/3/00, see whole document, particularly Figs. 1A-1B, 2, 6, 7, 11A-11B; Claims 1-26; column 6, lines 49-67; column 7, lines 1-35; column 8, lines 3-12; columns 9-11) recites adenoviral vectors which have left and right ITRs, one or more adenoviral genes essential for replication (which can be E4, E1a and E1b, etc.) and a packaging signal located at the right end of the adenoviral gene that is 3' to a termination signal of the heterologous gene inserted into said vector. Lieber et al. also recites insertion of an insulator sequence 5' of the first transcription unit of the viral vector and 3' of the left ITR element, use of a SV40 polyadenylation signal sequence to terminate transcription of the gene of interest, insertion of a therapeutic gene into the vector, viral particles containing the vectors and eucaryotic cells transfected with the vectors. With regard to the limitations of claim 2, it is noted that Lieber et al. inserts a insulator sequence 3' of the packaging signal but 5' of the heterologous promoter and hence would be within 3,000 nucleotides of the transcription start site of the transcription unit (See Fig. 11A). Lieber et al. therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 7-15, 20-22 and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Crystal et al.

Applicants' invention is as described in the above 102(e) rejections. Additionally, in claim 7, applicants recite that the insulating sequence is a SV40 early polyadenylation signal sequence.

Crystal et al. (US Patent 6,013,638, issued 1/11/00, see whole article, particularly Figs. 1, 3 and 4, column 2, lines 32-50; columns 3-5; Example 2) recites adenoviral vectors comprising a therapeutic gene (CFTR or α1 AT, etc.), a deleted E3 region, comprising at least one interfering genetic element (ITRs) and comprising at least one transcription unit (i.e. a CFTR gene, pIX gene, E2 gene or E4 gene, etc.) wherein at least one insulating sequence (i.e. a termination sequence or polyadenylation signal sequence) is located 5' to the transcription initiation site of said transcription unit and 3' to the left hand ITR. Crystal et al. recites adenoviral vectors further comprising 5' and 3' ITRs, a packaging signal, a SV40 early polyadenylation signal sequence operably linked to a CFTR gene, a gene essential for replication (i.e. E2 or E4 etc.), viral particles comprising the vectors and eukaryotic cells containing the vectors. With regard to claim 2, it is noted that the termination sequence at the end of the CFTR gene is less than 3,000 nucleotides 5' to the transcription initiation site of, for

example, the pIX transcription unit and the deletion of the E1 region is a deletion 5' to the termination sequence. Crystal et al. therefore teaches the claimed invention.

Claims 1-5, 8-15, 20-21 and 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Vassaux et al.

Applicants' invention is as described in the above 102(e) rejections.

Vassaux et al. (Cited by applicants, Gene Therapy, 1999, Vol. 6, pp. 1192-1197, see whole article, particularly the abstract, paragraph bridging columns 1 and 2 on p. 1192; Figure 1; paragraph bridging pp. 1194-1195; paragraph bridging pp. 1195-1196) recites adenoviral vectors, particles containing said vectors and eucaryotic cells transfected with said particles wherein said vectors comprise left and right ITRs, a packaging signal (and any naturally occurring interfering genetic elements contained therein), a insulator sequence (bovine growth hormone transcription stop signal designated "Ins") flanking the ETA expression cassette (the first transcription unit from the 5' end of the vector wherein said ETA expression cassette contains a TK polyadenylation signal) and genes essential for replication such as E4. With regard to claim 15, the vector contains an E1 deletion which is 5' to the termination signal present in the E3 gene in the vector. Vassaux et al. therefore teaches the claimed invention.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-5, 8-13, 15-25 and 27-30 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 13-14, 16-45, 47-51, 58-59, 62-64 and 67-83 of copending Application No. 10/081,969 (hereafter the '969 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are generic to all that is claimed in the '969 patent. That is the claims in the '969 application fall entirely within the scope of the instant claims and would anticipate the instant claims. For example, claim 1 of the '969 application recites an adenoviral left ITR (a interfering genetic element), a termination signal sequence (an insulating sequence), an E2F responsive promoter operably linked to a gene essential for replication (i.e. E4, E1, etc. which at least one transcription unit), an adenoviral packaging signal and a right ITR. Therefore the '969 application recites a viral vector having at least one interfering genetic element and comprising at least one transcription unit, wherein at least one insulating sequence is located 5' to the transcription initiation site of said transcription unit and 3' to said interfering genetic element. The limitations in the dependent claims as to polyadenylation sites, essential genes, therapeutic genes expressed, etc. are encompassed within the instant claims reciting broadly viral (adenoviral) vectors

containing any therapeutic gene, any polyadenylation or termination sites, tissue specific promoters, etc.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-5, 8-13, 15-25 and 27-30 are directed to an invention not patentably distinct from claims 1-11, 13-14, 16-45, 47-51, 58-59, 62-64 and 67-83 of commonly assigned 10/081,969. Specifically, the claims are not patentably distinct for the reasons outlined in the above obviousness type double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 10/081,969, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon

the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15 and 19 (and dependent claims) are vague in that there is no antecedent basis for the term "the termination signal sequence" in claim 11.

Claims 17 and 18 are vague in that it is unclear what nucleotides are being deleted. Applicants recite deletions of nucleotides 189 to 551 and 103 to 551 but it is unclear what these nucleotides are in relation to, i.e. 189 to 551 from the left terminus of the adenoviral genome or in relation to some other viral gene or locus?

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
December 20, 2004

DAVID GUZO
PRIMARY EXAMINER